The golden years

Pippias, M.

Chapter 11

Long-term kidney transplant outcomes in primary glomerulonephritis: analysis from the ERA-EDTA Registry

Maria Pippias, Vianda S. Stel, Nuria Aresté-Fosalba, Cécile Couchoud, Gema Fernandez-Fresnedo, Patrik Finne, James G. Heaf, Andries Hoitsma, Johan De Meester, Runolfur Pálsson, Pietro Ravani, Mårten Segelmark, Jamie P. Traynor, Anna Varberg Reisæter, Fergus J. Caskey and Kitty J. Jager

Transplantation. 2016 Sep; 100(9): 1955-62

Abstract

Background: We evaluated the 15-year kidney allograft survival in patients with primary glomerulonephritis and determined if the risk of graft loss varied with donor source within each glomerulonephritis group.

Methods: Using data from the ERA-EDTA Registry, Kaplan-Meier, competing risk and Cox regression analyses were performed on adult, first kidney transplant recipients during 1991-2010 (N=14,383). Follow-up was set to 31st December 2011. Adjustments for pre-transplant dialysis duration, sex, country and transplant era were made. 'Death-adjusted graft survival' was assessed in patients with glomerulonephritis and compared to those with autosomal dominant polycystic kidney disease (ADPKD), in which the native kidney disease cannot recur. Additionally, death-adjusted graft survival was compared between living and deceased donor transplants within each glomerulonephritis group.

Results: All glomerulonephritides had a 15-year death-adjusted graft survival probability above 55%. The 15-year risk of death-adjusted graft failure compared to ADPKD ranged from 1.17 (95%CI: 1.05; 1.31) for immunoglobulin A nephropathy to 2.09 (95%CI: 1.56; 2.78) for membranoproliferative glomerulonephritis type II. The expected survival benefits of living over deceased donor transplants were not present in membranoproliferative glomerulonephritis type I (HRa: 1.08, 95%CI: 0.73; 1.60) or type II (HRa: 0.90, 95%CI: 0.32; 2.52) but present in immunoglobulin A nephropathy (HRa: 0.74, 95%CI: 0.59; 0.92), membranous nephropathy (HRa: 0.47, 95%CI: 0.29; 0.75) and focal segmental glomerulosclerosis (HRa 0.69, 95%CI: 0.45; 1.06).

Conclusions: This large European study shows favourable long-term kidney graft survival in all primary glomerulonephritides, although this remains lower than graft survival in ADPKD, and confirms that the reluctance to use living donors in some primary glomerulonephritides remains unfounded. These data will further inform prospective renal transplant recipients and donors during pre-transplant counselling.

Introduction

Glomerulonephritis (GN) is a leading cause of ESRD and subsequent need for RRT (226). Despite the high prevalence of ESRD secondary to primary GN, long term transplant outcomes, particularly in the less common glomerulonephritidies, remain inconclusive. A major cause of graft loss in patients with primary GN is post-transplant disease recurrence (PTDR), i.e. the return of the original disease in the kidney allograft. The incidence of PTDR, typically a late complication, has paradoxically increased (227), as short-term graft survival has improved (228, 229). The risk of resulting graft loss varies considerably depending on the type of GN (229) but also within individual GNs there is a substantial disparity in the reported rate of graft loss (230). These reported differences may be explained in part by variations in study designs (231, 232). Therefore, there is the need for a large study to investigate long-term outcomes in transplant recipients with primary GN.

Furthermore, due to the genetic nature of some primary GNs, it remains unclear whether the recipients of living-related donor (LRD) transplants are at a greater risk of graft loss from PTDR compared to recipients of deceased donor (DD) transplants (203, 207, 232, 233). Most international guidelines recommend the use of LRD transplants in patients with primary GN, though with limited supporting evidence (14, 203, 207, 233). The conflicting evidence regarding the risk of graft loss from primary GN, in particular due to kidney donor type, makes pre-transplant counselling difficult for the transplant team and the prospective donor-recipient pair.

Using the ERA-EDTA Registry database, we aimed, first to quantify the 15-year kidney allograft survival probability in patients with primary GN and secondly to compare the risk of graft failure in renal transplants in patients with primary GN in which the native renal disease can recur to those with autosomal dominant polycystic kidney disease (ADPKD) in which the kidney disease cannot recur. Third, we aimed to determine if the risk of kidney allograft loss in those with primary GN differed across donor types.

Methods

Data collection

The ERA-EDTA Registry collects data on patients undergoing renal replacement therapy from national and regional renal registries on an annual basis (234). Seventeen renal registries which provided accurate and complete data from at least 1994 were included:

Austria, Dutch- and French-speaking Belgium, Denmark, Finland, Greece, Iceland, Norway, the Spanish regions of Andalusia, Asturias, Basque Country, Catalonia, Cantabria and Valencia, Sweden, the Netherlands and UK: Scotland.

We included patients aged 18 years and older at the time of receiving a first kidney transplant, between 1991 and 2010, with one of the following primary GNs (ERA-EDTA Registry codes in brackets): immunoglobulin A nephropathy (IgAN, 12), membranoproliferative glomerulonephritis (MPGN) type I (15), MPGN type II (13), membranous nephropathy (MN, 14) and focal segmental glomerulosclerosis (FSGS, 17). Patients with a primary renal diagnosis where the exact GN type could not be determined i.e. 'glomerulonephritis, histologically not examined' (10), 'crescentic (extracapillary) glomerulonephritis' (16) and 'glomerulonephritis; histologically examined, not given above' (19) formed a further group called 'other'.

Statistical Analysis

The primary outcome was 'death-adjusted graft survival' where graft failure was the event and the analyses were adjusted for death with a functioning graft. The adjustment for death with a functioning graft depended on the type of analyses; either by treating death as a competing risk or by censoring for death with a functioning graft (see below) (60). The secondary outcome was 'graft survival' in which both death with a functioning graft and graft failure were events. In all survival analyses, the date of kidney transplantation was taken as the starting point, the end of follow-up time was set at 31st December 2011 and all analyses were censored for loss to follow-up.

Unadjusted 5-, 10- and 15-year graft survival probabilities with 95% confidence intervals were obtained. First, the cumulative incidence competing risk method was used to calculate death-adjusted graft survival (where death with a functioning graft was treated as a competing risk, as the events graft failure and death with a functioning graft are mutually exclusive) (60). Second, the Kaplan-Meier method was used to calculate graft survival probabilities.

Two models were used to examine the risk of death-adjusted graft failure, (i.e. censored for death with a functioning graft) and the risk of graft failure (60):

Model 1: Individual types of GN compared with ADPKD

Cox regression analysis was performed comparing the risk of both death-adjusted graft failure and graft failure for each individual GN group with the ADPKD control group

considering all the donor types combined. The control group consisted of patients aged 18 years and older at the time of receiving a first kidney transplant within the same time period with a primary renal diagnosis of ADPKD. As the ERA-EDTA Registry database does not include information on the causes of graft loss, we assumed that most of the additional graft loss in the GN group compared with graft loss in patients with ADPKD, in which the native kidney disease cannot recur, could be attributed to PTDR. The Chi-squared test and Mann-Whitney U test were used to compare the characteristics of the cases and ADPKD controls.

To verify our choice of ADPKD as an appropriate control group a sensitivity analysis was performed by repeating the multivariable Cox regression analysis of model 1 using a different control group, consisting of all adult first kidney transplant recipients with a primary renal disease of pyelonephritis (ERA-EDTA codes 20-25, 29), congenital anomalies of the kidney and urinary tract (CAKUT, 30-34, 39) or tubulo-interstitial nephritis (TIN, 60-61, 63, 66).

Model 2: Living donor (LD) versus DD kidney transplantation by glomerulonephritis
A Cox regression model was used to compare the risk of both death-adjusted graft failure and graft failure between LD, LRD and living unrelated donor (LUD) grafts to the corresponding DD grafts for each GN group individually. In all cases the DD transplants within the GN group were used as the control (i.e. IgAN LRD compared with IgAN DD grafts).

For both models 1 and 2, adjusted hazard ratios (HRa) with 95% confidence intervals were calculated at 5-, 10- and 15-years post-transplant with adjustments for time on dialysis, age at transplantation, sex, country and the transplant era (1991-1995, 1996-2000, 2001-2005, 2006-2010). In model 1, additional adjustments were made for donor type (living versus deceased donor).

A two-tailed p-value of less than 0.05 was considered statistically significant. Analyses were performed using SAS version 9.3 and R version 3.0.2.

Results

Within the study period, 55,741 first kidney transplants were performed in adult recipients, of which 14,383 recipients had a potential diagnosis of primary GN, 6,327 with a definitive diagnosis of primary GN, (IgAN, MPGN I, MPGN II, MN and FSGS) were included along with 8,056 recipients in the group termed 'other'. Median follow-up time was 74.3 months (IQR: 36; 124) for transplant recipients with primary GN.

	All GN groups combined	IgAN	MPGN I	MPGN II	MN	FSGS	Other	ADPKD	p-value, all GNs vs ADPKD
Total number	14383	3778	701	153	708	987	8056	7187	
Age at first transplant, yrs, median, (IQR)	47.5 (36.5; 57.5)	44.9 (35.0; 54.8)	45.3 (33.4; 55.7)	40.5 (31.1; 50.5)	51.7 (41.2; 60.7)	47.2 (36.5; 57.3)	48.6 (37.4; 58.6)	54.1 (47.9; 60.1)	<0.001
% Male	71.2	78.8	63.5	58.8	74.3	67.1	68.7	54.9	<0.001
Dialysis duration, yrs, median, (IQR)	1.63 (0.74; 3.16)	1.31 (0.58; 2.65)	1.76 (0.78; 3.27)	1.88 (0.94; 3.42)	1.80 (0.88; 3.19)	1.57 (0.69; 3.10)	1.78 (0.84; 3.37)	1.68 (0.77; 3.15)	0.1
Pre-emptive transplant (%)	71.2	78.8	63.5	58.8	74.3	67.1	68.7	54.9	0.003
RRT modality day 91 (%)									
HD	61.2	51.9	59.7	58.2	60.5	63.3	65.7	66.6	<0.001
PD	27.6	34.2	29.0	34.0	28.7	25.0	24.6	21.5	
Transplant	10.5	13.3	10.2	7.2	10.0	11.1	9.2	11.4	
Transplant type (N / %)									
LD***	3150 / 21.9	1073 / 28.4	147 / 21.0	25 / 16.3	149 / 21.1	194 / 19.7	1562 / 19.4	1145 / 19.1	<0.001
LRD	1965 / 13.7	625 / 16.5	72 / 10.3	17 / 11.1	65 / 9.2	142 / 14.4	1044 / 12.9	451 / 6.3	
LUD	495 / 3.5	171 / 4.5	15 / 2.1	1 / 0.7	36 / 5.1	41 / 4.2	231 / 2.9	335 / 4.7	
DD	10784 / 75.0	2626 / 69.5	539 / 76.9	121 / 79.1	536 / 75.7	790 / 80.0	6172 / 76.6	5811 / 80.9	
Unknown	449 / 3.1	79 / 2.1	15 / 2.1	7 / 4.6	23 / 3.4	3 / 0.3	322 / 4.0	225 / 3.1	
Transplant era (%)									
1991-1995	21.1	14.5	23.4	31.4	17.4	11.6	25.3	15.8	<0.001
1996-2000	25.4	22.8	26.5	23.5	26.4	18.3	27.4	23.7	
2001-2005	26.8	29.6	26.4	23.5	24.4	31.1	25.3	27.2	
2006-2010	26.7	33.2	23.7	21.6	31.8	39.0	22.0	26.7	

IgAN: immunoglobulin A nephropathy; MPGN: membranoproliferative glomerulonephritis; MN: membranous nephropathy; FSGS: focal segmental glomerulonephritis; GN: glomerulonephritis; ADPKD: autosomal dominant polycystic kidney disease; RRT: renal replacement therapy; HD: haemodialysis; PD: peritoneal dialysis; ***LD: living donor (contains living-related, living-unrelated and living-unknown); LRD: living related donor; LUD: living unrelated donor; DD: deceased donor.

Table 11.1 Baseline characteristics of individual and aggregated primary glomerulonephritis and ADPKD groups.

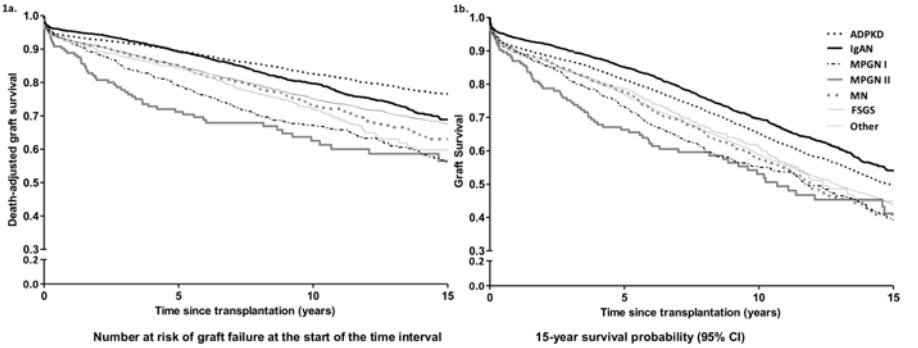
Patient Characteristics

Patient characteristics are presented in Table 11.1. Overall, the median age of patients in the GN group was 47.5 years (IQR: 35.6; 57.5) at the time of transplantation and 71.2% were male.

Survival probabilities

The death-adjusted graft survival and graft survival by primary GN, 'other' GNs and ADPKD are presented in Figure 11.1 (left and right panels respectively). MPGN I and II had the lowest 15-year death-adjusted graft survival probabilities (56.7 and 56.5% respectively), while IgAN had the highest 15-year death-adjusted graft survival (68.9%) of all GNs. The 15-year death-adjusted graft survival probability for those with a PRD of ADPKD was 76.6%.

Figure 11.1. Graft survival probability of first kidney transplant recipients by glomerulonephritis group and ADPKD for (a) death-adjusted graft survival, using the cumulative incidence competing risks method (left panel) and for (b) graft survival, using the Kaplan-Meier method (right panel).



Number at risk of graft failure at the start of the time interval

PRD	At transplant	5 years	10 years	15 years
IgAN	3778	2334	1045	316
MPGN I	701	415	210	68
MPGN II	153	86	47	21
MN	708	408	186	56
FSGS	987	530	205	50
Other	8056	5019	2596	926
ADPKD	7181	4180	1976	608

15-year survival probability (95% CI)

Death-adjusted graft survival	Graft survival
68.9 (66.6, 71.3)	54.9 (52.4, 57.3)
56.7 (51.8, 61.6)	40.7 (35.8, 45.5)
56.5 (49.5, 67.6)	41.0 (31.1, 50.6)
63.0 (58.0, 68.1)	40.9 (35.5, 46.1)
59.8 (54.7, 65.0)	44.4 (39.2, 49.5)
67.2 (66.1, 68.8)	43.7 (42.1, 45.2)
76.6 (75.2, 78.0)	49.6 (47.7, 51.4)

Footnote: IgAN: immunoglobulin A nephropathy; MPGN: membranoproliferative glomerulonephritis Type I or II; MN: membranous nephropathy; FSGS: focal segmental glomerulosclerosis; ADPKD: autosomal dominant polycystic kidney disease; PRD: primary renal disease; 95%CI: 95% confidence interval.
Other contains the PRD groups: 'glomerulonephritis, histologically not examined', 'crescentic (extracapillary) glomerulonephritis' and 'glomerulonephritis; histologically examined, not given above'.

Model 1: Individual type of GN compared to ADPKD

The 5-, 10- and 15-year adjusted relative risks of death-adjusted graft failure and graft failure for individual primary GNs and the 'other' group as compared with ADPKD are presented in Figure 11.2 and Supplementary Figure 11.1 respectively. All GNs had a greater risk of death-adjusted graft failure compared with ADPKD, with the exception of IgAN. For IgAN there was no difference in the risk of death-adjusted graft failure until 10 years post-transplant, thereafter the risk of graft loss was greater in the IgAN group.

Model 2: LD versus DD transplants by GN

Figure 11.3 and Supplementary Figure 11.2 present the 5-, 10- and 15-year adjusted risk of death-adjusted graft failure and graft failure for LD compared to DD transplants, by individual GNs respectively. Death-adjusted graft failure for the LD transplants in the IgAN, MN and 'other' group was lower than for the corresponding DD transplants. However this graft survival advantage became less apparent when divided into the smaller LRD and LUD subgroups (Figure 11.4 and Supplementary Figure 11.3). MPGN I and II showed no difference in death-adjusted graft failure when LD and DD transplants were compared. Within the FSGS group, LD and more specifically LRD transplants had a lower risk of death-adjusted graft failure at 5 and 10 years compared with the FSGS DD transplants but not at 15 years.

Sensitivity analysis

Repeating the analysis from model 1 with a control group comprising kidney transplant recipients with pyelonephritis, CAKUT or TIN produced similar results within the primary GN groups (Supplementary Table 11.1).

Footnote Figure 11.2 (overleaf left panel). Adjusted hazard ratios presented with 95% confidence interval in brackets and adjusted for dialysis vintage, age at start of transplantation, sex, country, donor type (living versus deceased) and the transplant era (1991-1995, 1996-2000, 2001-2005 and 2006-2010).

Footnote Figure 11.3 & 11.4 (overleaf middle and right panels respectively). ***Living donors (LD) includes living-related donors (LRD), living-unrelated donors (LUD) and living donors of unknown source compared to deceased donor (DD) transplants by PRD. IgAN: immunoglobulin A nephropathy; MPGN: membranoproliferative glomerulonephritis type I or II; MN: membranous nephropathy; FSGS: focal segmental glomerulosclerosis.
Adjusted hazard ratios are presented with the 95% confidence interval in brackets and adjusted for dialysis vintage, age at start of transplantation, sex, country and the transplant era (1991-1995, 1996-2000, 2001-2005 and 2006-2010). LUD transplants in MPGN II group are not presented due to the small sample size.

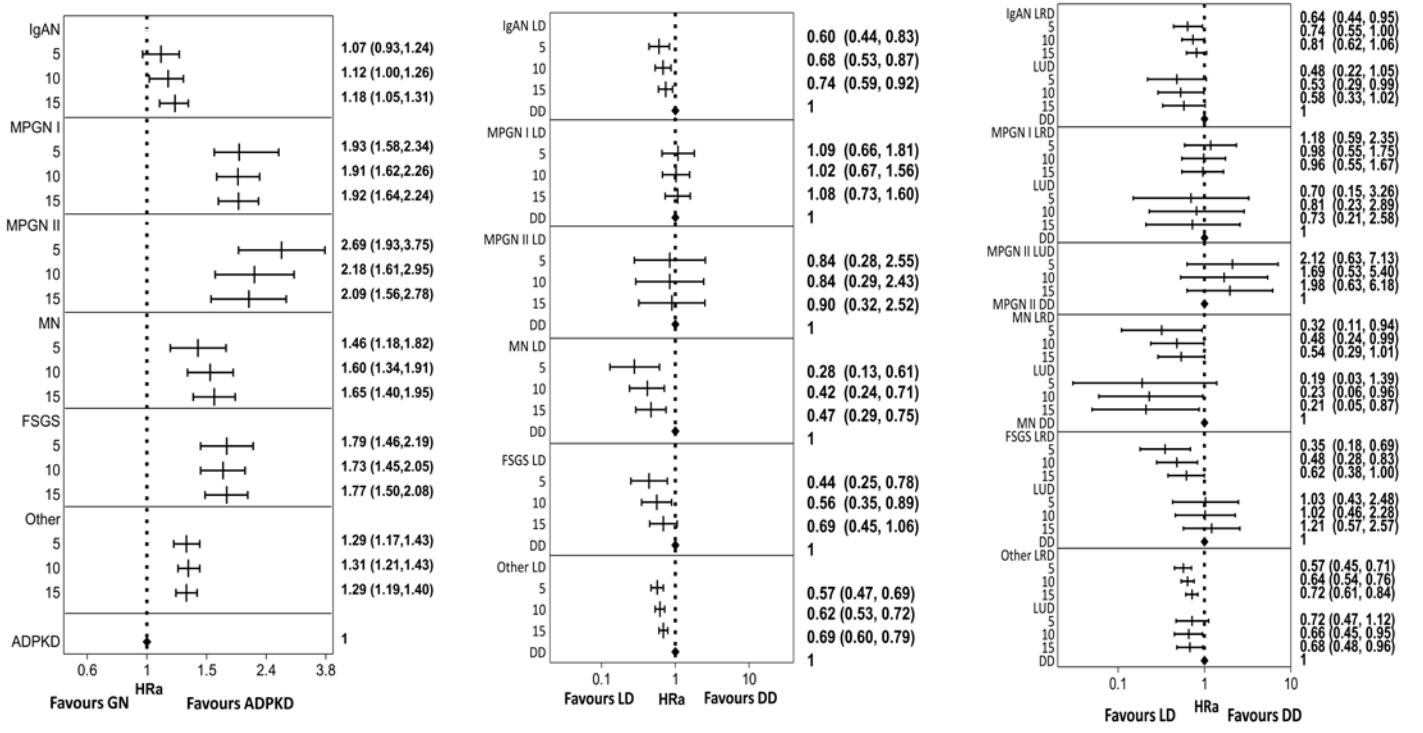


Figure 11.2 (left panel). Five-, 10- and 15-year adjusted relative risk of death-adjusted graft failure for each glomerulonephritis group as compared to ADPKD, presented for all kidney transplant donor types. Figure 11.3 (middle panel). Five-, 10- and 15-year adjusted relative risk of death-adjusted graft failure for each living kidney transplant donor as compared to deceased donor type, presented for each glomerulonephritis group. Figure 11.4 (right panel). Five-, 10- and 15-year adjusted relative risk of death-adjusted graft failure for each living kidney transplant donor type (living related and living unrelated) as compared to deceased donor type, presented for each glomerulonephritis group.

Discussion

In this large cohort of 6,327 kidney transplant recipients with a PRD of primary GN and a long follow-up period we found that all GN types had a 15-year death-adjusted graft survival probability of over 55%. Additionally, we compared graft loss in patients with various primary GNs, in which the return of the original disease in the kidney allograft can occur, to those with ADPKD. All types of primary GN had a greater risk of death-adjusted graft failure compared to ADPKD, with the exception of IgAN, which had a similar risk of death-adjusted graft failure and graft failure up to 10 years post transplantation. In addition, the expected survival advantage normally seen in LD kidney transplants over DD transplants was not apparent in the MPGN I and II groups, but present in the IgAN, MN and FSGS groups.

Immunoglobulin A Nephropathy

It is well known that kidney transplant recipients with IgAN have a better short-term graft survival (235), possibly due to immunological benefits, though recent studies with long-term follow-up have reported that the superior graft outcomes initially enjoyed by IgAN recipients may be lost between 8 and 12 years post-transplant (236). To date, our study contains the largest number of kidney transplant recipients with IgAN and a long follow-up time. The results indicate that IgAN may eventually have a detrimental effect on long-term kidney allograft outcome.

From previous publications it is not entirely clear whether the risk of PTDR in LD transplants is greater than in DD transplants in IgAN, predominantly due to the small sample sizes of the available studies (237). Although we cannot confirm the causes of graft loss in our cohort, the results of our large study clearly show that LD transplants in IgAN have a lower risk of death-adjusted graft failure compared to DD transplants in IgAN. Thus, our findings support the notion that there need be no contraindications to LD kidney transplantation in patients with IgAN.

Membranoproliferative Glomerulonephritis I and II

When comparing the living donor transplant subtypes to DD transplants in both MPGN I and II, the expected survival advantage normally seen for LD transplants was no longer apparent, though the outcome was no worse than for DD transplants. Neither MPGN I or MPGN II are listed as a contraindication to LD kidney transplantation in a number of transplant guidelines (207, 233). However, some studies still recommend caution when accepting LRD grafts for patients with MPGN II due to a higher risk of PTDR (207). The published data on PTDR in MPGN I with respect to donor source are limited and conflicting (238-240). In contrast to our findings a study by Angelo et al. based on the

United Network for Organ Sharing database, reported better graft survival for LD kidney transplants (241). It is difficult to draw any firm conclusions or compare the results with our findings for a number of reasons. First, our study included only adult patients; differences in outcomes between adult and paediatric populations, particularly for MPGN II, have previously been described (242). Second, neither study had access to biopsy data. It has been postulated that the disease severity as manifested by the presence of crescents on the initial native kidney biopsy rather than the type of disease alone predicts transplant outcomes (243), further supporting the argument that the heterogeneity of most types of GNs makes any predictions of outcome difficult. Finally, whilst this study and that of Angelo et al. represent the largest published cohorts of transplanted patients with MPGN II, the rarity of this disease and thus the relatively small sample size, still makes it difficult to compare outcomes from LRD and LUD grafts.

Membranous Nephropathy

The ANZDATA registry reported 12.5% renal graft loss from recurrent MN at 10 years post-transplant (227). Accordingly, we would have expected a higher risk of death-adjusted graft failure in the MN group compared with the ADPKD group, which was indeed the case.

Since the identification of M-type phospholipase A2 receptor autoantibodies (PLA2R) as potentially pathogenic in idiopathic MN (244), several studies have implicated PLA2R in the pathogenesis of recurrent idiopathic MN (245). In a study of 23 transplant recipients with idiopathic MN, Andresdottir and Wetzels reported a cumulative rate of PTDR at 3 years of 70% in LRD and 21% in LUD transplants (246). They hypothesized that genetic factors, such as PLA2R may therefore play an important role in disease recurrence. Based on this hypothesis, we would expect to see a worse graft survival in LRD transplants compared with DD transplants in patients with MN, however we found that at 5- and 10-years follow-up the LRD transplants in the MN group had a lower risk of death-adjusted graft failure. From our data it is not possible to distinguish idiopathic MN from secondary MN. The possibility that some cases of secondary MN were reported as idiopathic MN and the small sample size in this study may have masked any potential graft survival outcomes from differing LD types.

Focal Segmental Glomerulosclerosis

FSGS is the most frequently recurring primary GN after kidney transplantation, developing in approximately 30% of transplants (247). Our study found that those with a first kidney transplant for ESRD secondary to FSGS were, by 15 years, 77% more likely to experience death-adjusted graft failure compared with ADPKD.

Transplantation guidelines do not exclude LRD transplants in patients with recurrence (207). Many studies report a better graft survival in LD transplants compared with DD transplants in patients with FSGS (248-250), particularly in paediatric cohorts (251). The majority of studies examining PTDR in FSGS include only paediatric or mixed adult and paediatric cohorts, whereas our study comprised only adult recipients. Our results suggest that in an adult European population, LD and in particular LRD kidney transplants have a reduced risk of death-adjusted graft failure compared with DD transplants in patients with FSGS.

Limitations

Within this study we report on the long term graft survival of a large cohort of transplant recipients with primary GN. We additionally investigated the risk of graft loss between patients with ESRD secondary to primary GN, in which the native kidney disease can recur in the transplanted kidney and in patients with ADPKD in which the native kidney disease cannot recur in the transplanted kidney. We do not have the causes of graft loss in our cohort. Therefore, we assumed that most of the additional graft loss in the GN group compared with the ADPKD group could be attributed to PTDR. It should be noted, however, that other factors could be responsible for the increased risk of graft loss, such as the type of immunosuppression used and the pre-transplantation clinical status of the patients. However information regarding these potential confounding factors are not available within the ERA-EDTA Registry data. Some studies have observed better kidney allograft outcomes in patients with ADPKD compared with other causes of ESRD (252), which may have resulted in overestimation of the relative risk of graft loss when comparing patients with primary GN to those with ADPKD. Using different control groups we obtained similar results supporting the assumption that the ADPKD group is suitably representative of a control group with no possibility of PTDR.

A large proportion of the patients had a diagnosis of GN but not of one of the five primary GNs (IgAN, MPGN I, MPGN II, MN and FSGS), on which this study focused. These patients were categorised as 'other' on the basis that the assigned PRD codes ('glomerulonephritis, histologically not examined', 'crescentic (extracapillary) glomerulonephritis' and 'glomerulonephritis; histologically examined, not given above') did not provide any information as to the underlying type of GN. Although little can be said with regards to the clinical significance of this group, the fact that the results of this large group were not dissimilar to the other primary GN groups is reassuring.

In this study we also investigated the risk of graft loss between patients with ESRD

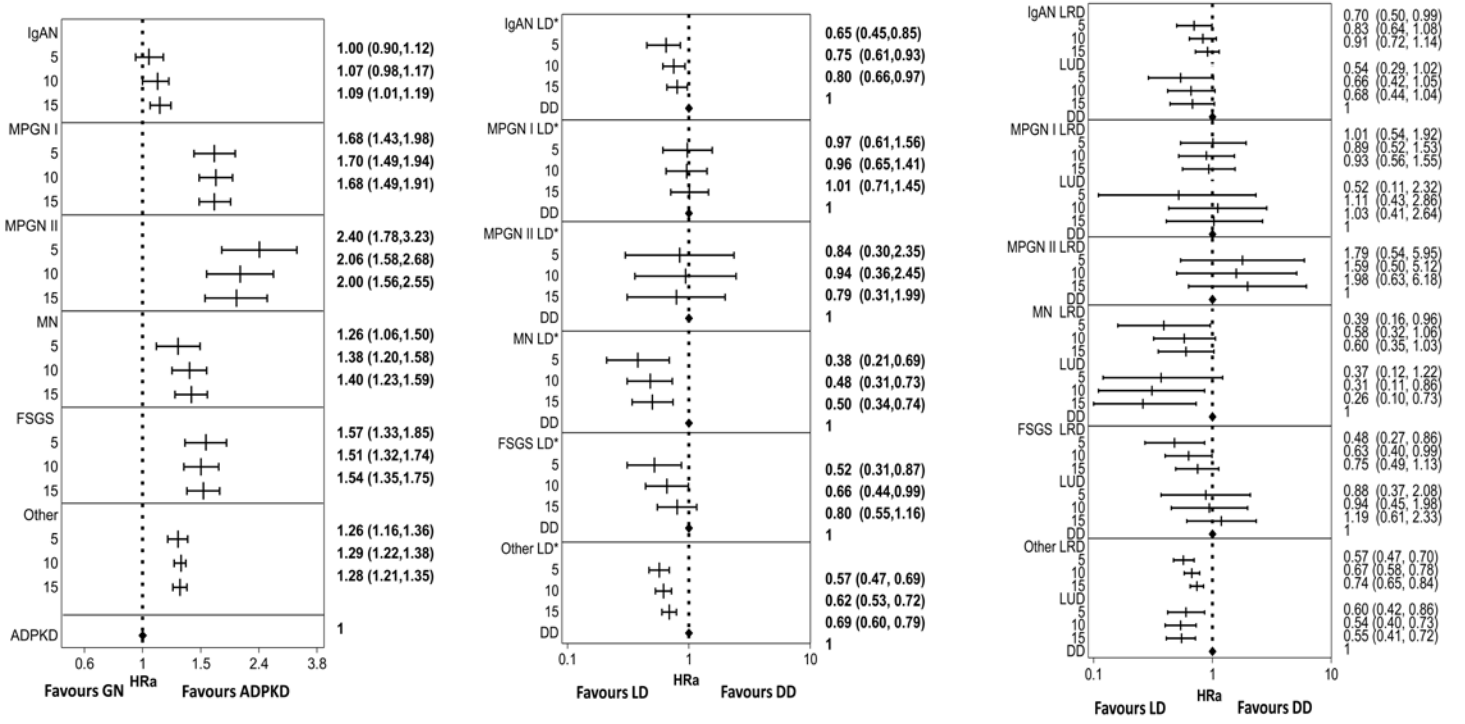
secondary to primary GN, who received a LD transplant compared to a DD transplant. Despite the very large sample size, the smaller living donor subgroups and in particular the lack of distinction between LRD and LUD in a proportion of our data, means that in some cases firm conclusions cannot be drawn. Some types of GN represent histological patterns rather than well-defined diseases and therefore we are unable to distinguish between certain GN subgroups using the current coding system. Furthermore, for a subset of patients a presumed diagnosis of ESRD secondary to GN is likely to have been applied without histological confirmation. The diagnosis of a specific form of GN may have been confirmed histologically once PTDR had occurred resulting in a change of the ERA-EDTA code. The reclassification of these patients could potentially have increased the number of patients in the cohort with graft loss secondary to GN, leading to an overestimation of the risk of graft loss.

Conclusion

This study has detailed the actual 15-year kidney allograft survival outcomes in patients with primary GN within a number of European countries. We found that all GN types had a 15-year death-adjusted graft survival probability of over 55%. Kidney transplants in patients with all types of primary GN, in which the native disease could recur, including IgAN, eventually have a greater risk of 15-year death-adjusted graft failure compared to ADPKD in which the original disease cannot recur. The expected graft survival advantage in LD over DD kidney transplants was apparent in patients with IgAN, MN and FSGS, although in FSGS the advantage was observed in LRD, while not in LUD, which may be due to the small sample size. In MPGN I and II, no survival benefit of LD versus DD grafts was seen. This study confirms that the reluctance to use LRD in some primary GNs remains unfounded. The results of this study are important to aid nephrologists in the pre-transplant counselling of potential renal transplant recipients and donors about risk of graft loss, particularly when considering donor type.

PRD	Follow up time (yrs)	N	Death-adjusted graft survival (95% CI)		Graft survival (95% CI)	
			Unadjusted	Adjusted	Unadjusted	Adjusted
IgAN	5	3778	0.72 (0.63; 0.81)	0.84 (0.73; 0.95)	0.63 (0.57; 0.70)	0.74 (0.67; 0.83)
	10	2332	0.79 (0.72; 0.87)	0.90 (0.81; 1.00)	0.70 (0.64; 0.75)	0.81 (0.74; 0.88)
	15	1044	0.84 (0.77; 0.92)	0.95 (0.86; 1.05)	0.73 (0.68; 0.79)	0.83 (0.77; 0.90)
MPGN I	5	701	1.48 (1.24; 1.77)	1.44 (1.20; 1.72)	1.20 (1.03; 1.40)	1.22 (1.05; 1.43)
	10	414	1.49 (1.29; 1.74)	1.46 (1.26; 1.70)	1.21 (1.06; 1.37)	1.24 (1.09; 1.42)
	15	209	1.50 (1.30; 1.72)	1.46 (1.27; 1.69)	1.21 91.07; 1.36)	1.25 (1.11; 1.41)
MPGN II	5	153	2.15 (1.58; 2.93)	1.98 (1.45; 2.71)	1.60 (1.20; 2.13)	1.65 (1.24; 2.20)
	10	85	1.80 (1.36; 2.39)	1.68 (1.27; 2.24)	1.35 (1.05; 1.74)	1.43 (1.11; 1.85)
	15	46	1.72 (1.31; 2.25)	1.62 (1.23; 2.12)	1.32 (1.04; 1.67)	1.41 (1.11; 1.79)
MN	5	708	1.05 (0.85; 1.30)	1.15 (0.93; 1.42)	0.99 (0.84; 1.17)	0.99 (0.83; 1.18)
	10	408	1.15 (0.97; 1.36)	1.24 (1.05; 1.48)	1.08 (0.94; 1.24)	1.05 (0.92; 1.21)
	15	185	1.19 (1.01; 1.39)	1.28 (1.09; 1.51)	1.12 (0.99; 1.27)	1.09 (0.96; 1.24)
FSGS	5	987	1.12 (0.94; 1.33)	1.29 (1.07; 1.56)	0.97 (0.84; 1.13)	1.11 (0.94; 1.30)
	10	529	1.19 (1.02; 1.38)	1.35 (1.16; 1.59)	1.00 (0.88; 1.13)	1.13 (0.99; 1.29)
	15	194	1.25 (1.09; 1.44)	1.40 (1.21; 1.63)	1.04 (0.92; 1.17)	1.16 (1.02; 1.31)
Other	5	8056	1.06 (0.98; 1.16)	1.05 (0.96; 1.14)	1.03 (0.96; 1.11)	0.97 (0.91; 1.05)
	10	5019	1.09 (1.01; 1.17)	1.06 (0.98; 1.14)	1.06 (1.00; 1.12)	0.99 (0.93; 1.05)
	15	2596	1.08 (1.01; 1.16)	1.05 (0.98; 1.12)	1.07 (1.02; 1.13)	1.00 (0.94; 1.05)
CAKUT, TIN or pyelonephritis		1	1	1	1	1

Supplementary Table 11.1. Results of the sensitivity analysis; Five-, 10- and 15-year unadjusted and adjusted relative risk of death-adjusted graft failure and graft failure for each glomerulonephritis group as compared to the control group (CAKUT, TIN or pyelonephritis).



Supplementary Figure 11.1 (left panel). Five-, 10- and 15-year adjusted relative risk of graft failure for each glomerulonephritis group as compared to ADPKD, presented for all kidney transplant donor types. Supplementary Figure 11.2 (middle panel). Five-, 10- and 15-year adjusted relative risk of graft failure for each living kidney transplant donor as compared to deceased donor type, presented for each glomerulonephritis group. *Living donors (LD) includes living-related donors (LRD), living-unrelated donors (LUD) and living donors of unknown type. Supplementary Figure 11.3 (right panel). Five-, 10- and 15-year adjusted relative risk of graft failure for each living kidney transplant donor type (living related and living unrelated) as compared to deceased donor type, presented for each glomerulonephritis group.